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Complicated appendicitis: Immediate operation or trial of nonoperative management?

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ABSTRACT

Background: The optimal treatment for complicated appendicitis remains controversial. We sought to compare clinical outcomes of patients with complicated appendicitis treated with an immediate operation or a trial of nonoperative management.

Methods: Adult patients (≥18 years) with complicated appendicitis were included. Patient characteristics and outcomes were compared between the immediate operation group and the nonoperative management group.

Results: A total of 101 patients met our inclusion criteria. Of those, 36 patients received an initial trial of nonoperative management with an 86.1% success rate. Patients who failed nonoperative management required significantly longer hospital stays than those in the immediate operation group (11 vs. 5 days). An immediate operation was performed in 65 patients. Open surgery was required in 9 patients (13.8%). Postoperatively, 7 patients (10.8%) required percutaneous drainage of intraabdominal abscess.

Conclusions: Nonoperative management was successful in the majority of patients with complicated appendicitis, whereas failure of nonoperative management was associated with prolonged hospital stay. Patients who underwent an immediate operation often required percutaneous drainage of intra-abdominal abscess.

Introduction

Acute appendicitis is one of the most common causes of abdominal emergencies in the United States. Acute appendicitis has increased in incidence over the years and now affects 9.4 per 10,000 people annually, resulting in about 300,000 cases per year.[1] The pathogenesis of acute appendicitis involves initial inflammation of the appendiceal wall leading to localized ischemia, necrosis, and perforation. Due to the inflammation and/or necrosis that occurs, the appendix is at risk for perforation and localized abscess or phlegmon formation, which is considered complicated or complex appendicitis.[2] Overall, about 30% of acute appendicitis cases in the United States are considered as complicated appendicitis.[1]

In patients with acute uncomplicated appendicitis, the standard of care is appendectomy, ideally within 24 h.[2] Previous prospective randomized studies showed that nonoperative management with antibiotics can be successful in the majority of patients with uncomplicated appendicitis who wish to avoid surgery and accept the risk of recurrent appendicitis.[4,5] In contrast, the optimal treatment for patients with complicated appendicitis remains controversial. Thus there is a significant disparity in treatment strategies among surgeons.[6–9] An immediate operative intervention is usually curative in this population, but can be difficult due to the inflammation and distortion of local anatomy, leading to increased complexity of the case. For those reasons, nonoperative management is a viable alternative for these patients and consists of antibiotic therapy with percutaneous drainage when appropriate.

While successful nonoperative management provides a favorable outcome in patients with complicated appendicitis, recent small retrospective studies have found results indicating that failure of nonoperative management is associated with significant

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morbidity, making the risk of initial trial of nonoperative management higher.[10,11] Therefore, this study aimed to analyze outcomes between patients who underwent an immediate operation or nonoperative management for complicated appendicitis. We hypothesize that the majority of patients undergoing nonoperative management would be successfully treated, however failure of nonoperative management would be associated with increased morbidity and prolonged hospital stay. We also hypothesized that patients who underwent an immediate operation would frequently require postoperative evaluation and intervention for intra-abdominal abscess.

Patients and methods

Study design and patients

This study is a retrospective cohort study at the LAC + USC Medical Center between May 2015 and November 2016. Adult patients (age ≥18 years) with complicated appendicitis were identified using a prospectively collected emergency general surgery database and included for analysis, with currently incarcerated and pregnant patients excluded. Complicated appendicitis was defined as perforation of the appendix, gangrenous appendicitis, and/or abscess/phlegmon noted on radiological studies upon hospital admission, operative reports, or pathology results of the surgical specimen. During the study period, all patients with complicated appendicitis were admitted to one of four Acute Care Surgery services and surgical decisions were made at the discretion of the attending surgeon as there was no institutional protocol implemented for the management of complicated appendicitis during the study period. However, all attending surgeons agreed with consensus on indications for an immediate operation in the patient with signs of generalized peritonitis, organ failure, or unevaluable patient. Patients who underwent an initial trial of nonoperative management were closely monitored in the surgical observation unit with serial physical examinations and laboratory tests. Postoperatively, patients were evaluated with computed tomography (CT) when signs and symptoms suggestive of intra-abdominal abscess (e.g. fever, abdominal pain, leukocytosis) developed.

Data collection and statistical analysis

After approval was obtained by the Institutional Review Board of the University of Southern California, inpatient medical records were reviewed for patient demographics, laboratory results, radiological findings, antibiotic therapy, and selection of operative or nonoperative management for complicated appendicitis. Subsequently, the study patients were divided into two groups, the immediate operation group (IOP group) and trial of nonoperative management group (NOM group). The primary outcome of interest was hospital length of stay (HLOS) in each study group. Secondary outcomes included the success rate of nonoperative management, the rate of open surgery, and postoperative infectious complications requiring diagnostic workup and percutaneous interventions.

Univariate analysis was performed to compare the patient characteristics and outcomes between the IOP vs NOM groups. Comparison between percentages of categorical variables was performed with Fisher Exact or Pearson's chi-squared test, while medians for continuous data were compared with the Mann-Whitney *U* test or the Kruskal-Wallis test when appropriate. All statistical analysis was performed using SPSS for Mac OS X version 23.0 (SPSS Inc. Chicago, IL).

Results

During a 19-months period, we identified a total of 101 patients who met our inclusion criteria. A median age was 41 years (interquartile range: 30–50) and 78.2% of the patients were male. The majority of study patients did not have any co-morbid conditions. Overall, 65 (64.4%) patients underwent an immediate operation. An initial surgical approach was laparoscopic in 62 patients (95.4%) and the procedure was converted to open surgery in 6 patients (Fig. 1). Ultimately, 9 patients required an open surgery (13.8%). Postoperatively, 18 (27.7%) patients required CT to evaluate for intraabdominal infectious complications and 7 (10.8%) patients received percutaneous drainage of intraabdominal abscess (range: postoperative 5–23 days).

The other 36 (35.6%) patients initially received nonoperative management with intravenous antibiotics. None of the patients in the NOM group were tachycardic upon admission to the ED. Otherwise, there was no significant difference in patient demographics, physical findings, or laboratory findings between the IOP group and NOM groups (Table 1). Complicated appendicitis was successfully treated without operative interventions in 31 patients (86.1% success rate) (Fig. 2). Out of these 31 patients, 5 (16.1%) patients were concordantly managed with percutaneous drainage of appendiceal abscess (hospital day 1–2). In addition, 10 (32.3%) patients required a repeat CT to look for the evolution of intra-abdominal abscess, of which 5 patients required percutaneous drainage between hospital day 4–8. The 5 patients who failed initial non-operative management were not significantly different in demographics, laboratory values, or physical examination than those who were successful with non-operative management (Table 2). All 5 patients who failed initial nonoperative management underwent an operation within 48 h after admission. The causes of failure included persistent abdominal pain, tachycardia, and fever despite antibiotics treatment. None of the patients developed generalized peritonitis or septic shock from complicated appendicitis while on a trial of nonoperative management. Three patients (60%) required an open appendectomy (laparoscopic converted to open surgery in 1 patient). Postoperatively, two patients (40%) required percutaneous drainage for intraabdominal abscess.

The median HLOS of the successful nonoperative patients was 5 days, which was equivalent to the patients in the IOP group. In contrast, the median HLOS in patients who failed nonoperative management was 11 days, which was significantly longer than the IOP group (Fig. 3). Only one patient in the NOM group required readmission within 30 days for emesis, but did not require any surgical interventions.

Discussion

While the recent consensus proposed by the World Society of Emergency Surgery advocates nonoperative approach as the initial treatment of complicated appendicitis, it still appears that surgeons continue to utilize both operative and nonoperative management, using clinical judgment based on clinical status, imaging, and co-morbid conditions to determine best practice.[3] To date, there are no large randomized prospective studies to conclusively determine the standard of care in this population.

In this study at a large tertiary care hospital, we have described the clinical course and outcomes of patients who received either an immediate operation or a trial of nonoperative management for complicated appendicitis. We found that less than 15% of the patients who underwent an immediate operation required an open surgery, though their postoperative course was often complicated by signs and symptoms which warranted additional radiographic

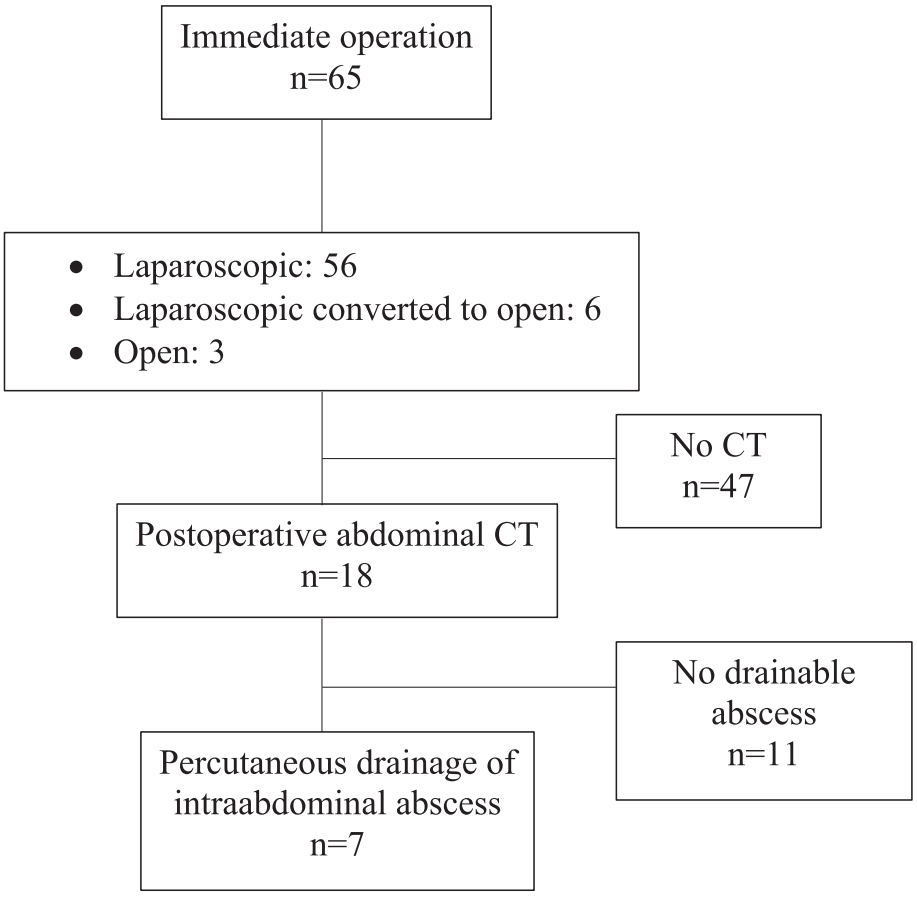

Fig. 1. Patient flow diagram in the immediate operation group. CT: computed tomography.

Table 1
Patient characteristics in two study groups.

Variables	Total patients (n = 101)	Immediate operation (n = 65)	Trial of NOM (n = 36)	p value
Median age (IQR)	41 (30–50)	41 (29–49)	41 (30–54)	0.52
Male gender (%)	78.2	80.0	75.0	0.56
Median Charlson Comorbidity Index (IQR)	0 (0–1)	0 (0–1)	0 (0–1)	0.56
Admission HR > 100 (%)	7.9	12.3	0	0.048
Median temperature (IQR)	37.2 (36.9–37.8)	37.3 (36.9–37.8)	37.0 (36.7–37.8)	0.12
Rebound tenderness (%)	29.5	34.5	20.0	0.16
Median WBC (IQR)	15.3 (12.9–18.8)	15.4 (12.4–18.8)	15.0 (13.0–19.2)	0.59
Diagnostic modality used				
CT (%)	81.2	70.8	100	<0.001
US (%)	39.6	44.6	30.6	0.17

NOM: nonoperative management, IQR: interquartile range, HR: heart rate.
WBC: white blood cell, CT: computed tomography, US: ultrasonography.

evaluation and percutaneous drainage of intraabdominal abscess. Patients initially managed nonoperatively had a high success rate. However, when nonoperative management failed, the patient frequently required an open surgery and experienced complicated postoperative course. Furthermore, their HOLS was significantly longer compared to those who had an immediate operation.

Out of the patients who received an immediate operative management in our study, 13.8% ultimately required open surgery, which is lower than the data reported in the study using the University HealthSystem Consortium (UHC) database.[12] In this large consortium-based study between 2006 and 2008, open appendectomy was performed slightly more frequently than laparoscopic appendectomy for complicated appendicitis (5323 vs. 5212 cases). In a smaller, randomized study by Mentula et al. however, the conversion rate from laparoscopic to open surgery for appendiceal abscess was reported as low as 10% in experienced hands.[13] While the learning curve and utilization of laparoscopy has increased in the past few decades, several studies in the interim have been published to support the feasibility and benefit of laparoscopic approach for complicated appendicitis.[14,15] A meta-analysis by Yu et al. showed that laparoscopic technique in complicated appendicitis resulted in reduction in surgical site infections, HLOS, and time to oral intake compared to open surgery.[16] Despite this plethora of data demonstrating successful outcomes with laparoscopy, it is important to emphasize that, in the current study including low-risk patients, over 25% of patients with an immediate operation underwent postoperative CT to look for deep organ space infection and 10% required percutaneous drainage, which is higher than seen in uncomplicated appendicitis cases.[12]

Our study demonstrates some key benefits of a trial of

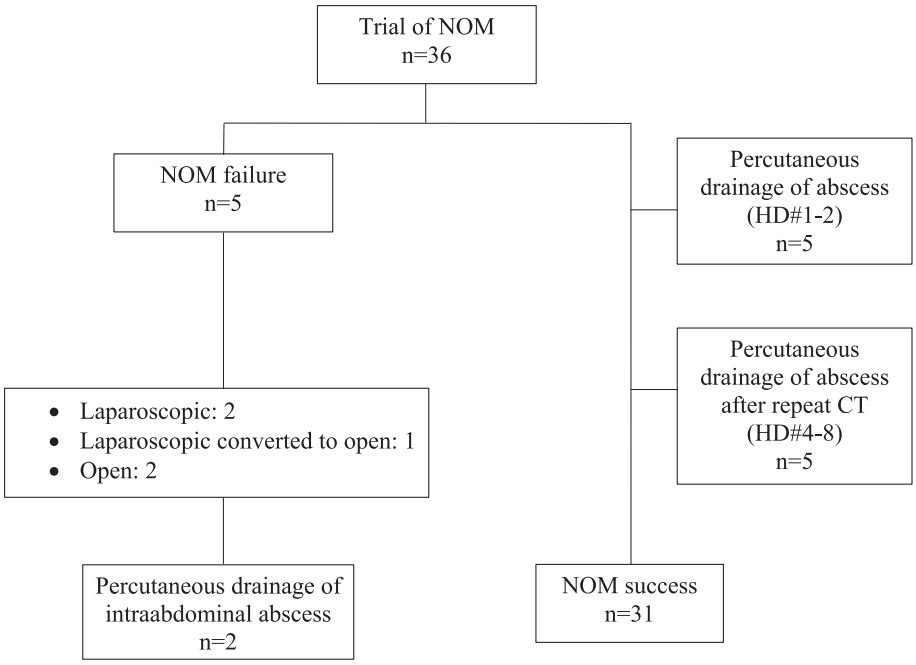

Fig. 2. Patient flow diagram in the nonoperative management group. NOM: nonoperative management, HD: hospital day, CT: computed tomography.

Table 2
Patients with successful and failure of nonoperative management.

Variables	Successful NOM (n = 31)	NOM failure (n = 5)	p value
Median age (IQR)	42 (30–55)	40 (29–47)	0.56
Male gender (%)	71.0	100	0.30
Median Charlson Comorbidity Index (IQR)	0 (0–1)	0 (0–1)	0.53
Median temperature (IQR)	37.0 (36.7–37.9)	36.7 (36.5–37.5)	0.28
Rebound tenderness (%)	16.0	40.0	0.25
Median WBC (IQR)	15.3 (12.9–19.4)	15.0 (12.6–20.5)	0.89

NOM: nonoperative management, IQR: interquartile range, HR: heart rate.
WBC: white blood cell.

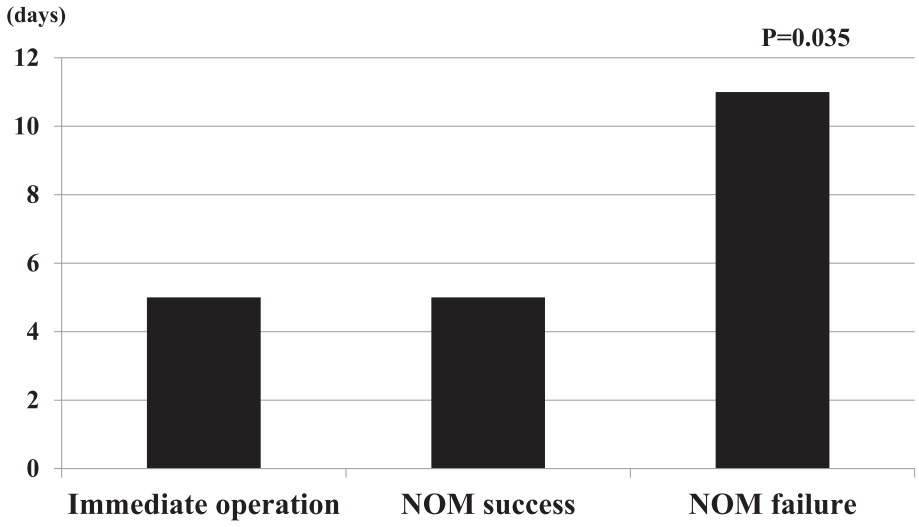

Fig. 3. Length of hospital stay. NOM: nonoperative management.

nonoperative management in patients with complicated appendicitis, while also showcasing the associated risks. Our results support the data in previous studies showing a high success rate of nonoperative management. A meta-analysis of 44 studies by Anderson et al. reported that the failure rate following nonoperative management in the patients with appendiceal abscess or phlegmon was 7.2%.[6] The success of non-operative management could be partly due to the frequent use of percutaneous drainage.

Interestingly, their data regarding the proportion of patients who required percutaneous drainage was similar to our study (19.7% vs. 16.1%). All of these patients were successfully treated with percutaneous drainage and did not require further operation, allowing for a minimally invasive treatment strategy. Furthermore, nonoperative management did not extend the HLOS of patients successfully managed nonoperatively. Our results similarly support a study by Simmilis et al., in 2010, which found no significant difference in HLOS for patients who received nonoperative versus an immediate operative management.[7]

On the other hand, the patients who failed nonoperative management had extended HLOS, a higher rate of open surgery, and a higher rate of post-operative complications necessitating percutaneous drainage. In our study, there were no other morbidities associated with failure of non-operative management. However, previous studies have found significant complications associated with failed nonoperative management. Young et al. looked at 35 patients with complicated appendicitis who underwent nonoperative management and found a 25.7% failure rate. Those who failed nonoperative therapy required open surgery and more than half (55.6%) required bowel resection, while patients who underwent an immediate appendectomy had a significantly lower incidence of bowel resection.[11] Thus, we believe that the patient should be informed about the risk of prolonged hospital stay, more extensive bowel resection, and postoperative infectious complications before initiating nonoperative management.

There are several limitations to this study. The biggest limitation is that these findings reflect the retrospective data collected from a single institution without standard guidelines for management of complicated appendicitis. A retrospective review of these cases cannot fully analyze treatment decisions and surgical approach. Further, the small sample size also limits the ability to generalize these findings to the general population. Particularly, the number of patients was too small to compare surgical outcomes between the IOP group and NOM failure group. Finally, this study did not capture data on patients undergoing interval appendectomy as, similar to other safety net hospitals, it is not uncommon that the patient is lost to follow up at our institution. Thus, we are unable to determine if patients in the NOM group had additional episodes of recurrent appendicitis and ultimately required an appendectomy.

Conclusions

This study demonstrates the risks and benefits of both immediate operation and a trial of nonoperative management in patients with complicated appendicitis. Given varied patient presentations and comorbid conditions, the treatment of complicated appendicitis remains a challenge without a clear algorithm. Therefore, we emphasize the importance of including the patient in the decision to manage operatively or nonoperatively given the significant differences in length of stay and possible complications. Ultimately, a future prospective randomized study conducted at multiple institutions is warranted to fully elucidate whether operative or nonoperative management is superior for treatment of complicated appendicitis.

Conflicts of interest

- None of the authors have any conflicts of interest to disclose
- Neither internal nor external financial support was used for this study

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amjsurg.2018.12.061.

References

1. Buckius MT, McGrath B, Monk J, Grim R, Bell T, Ahuja V. "Changing epidemiology of acute appendicitis in the United States: study Period 1993–2008. *J Surg Res*. 2012;175:185–190.
2. Bhangu A, Søreide K, Di Saverio S, Assarsson JH, Drake FT. Acute appendicitis: modern understanding of pathogenesis, diagnosis, and management. *Lancet*. 2015;386:1278–1287.
3. Di Saverio S, Birindelli A, Kelly MD, et al. WSES Jerusalem guidelines for diagnosis and treatment of acute appendicitis. *World J Emerg Surg*. 2016;11:34.
4. Vons C, Barry C, Maitre S, et al. Amoxicillin plus clavulanic acid versus appendicectomy for treatment of acute uncomplicated appendicitis: an open-label, non-inferiority, randomised controlled trial. *Lancet*. 2011;377:1573–1579.
5. Salminen P, Paajanen H, Rautio T, et al. Antibiotic therapy vs appendectomy for treatment of uncomplicated acute appendicitis: the APPAC randomized clinical trial. *J Am Med Assoc*. 2015;313:2340–2348.
6. Andersson RE, Petzold MG. Nonsurgical treatment of appendiceal abscess or phlegmon: a systematic review and meta-analysis. *Ann Surg*. 2007;246:741–748.
7. Simillis C, Symeonides P, Shorthouse AJ, Tekkis PP. A meta-analysis comparing conservative treatment versus acute appendectomy for complicated appendicitis (abscess or phlegmon). *Surgery*. 2010;147:818–829.
8. Cheng Y, Xiong X, Lu J, Wu S, Zhou R, Cheng N. Early versus delayed appendicectomy for appendiceal phlegmon or abscess. *Cochrane Database Syst Rev*. 2017;6:CD011670.
9. Deelder JD, Richir MC, Schoorl T, Schreurs WH. How to treat an appendiceal inflammatory mass: operatively or nonoperatively? *J Gastrointest Surg*. 2014;18:641–645.
10. Helling TS, Soltys DF, Seals S. Operative versus non-operative management in the care of patients with complicatedappendicitis. *Am J Surg*. 2017;214:1195–1200.
11. Young KA, Neuhaus NM, Fluck M, et al. Outcomes of complicated appendicitis: is conservative management as smooth as it seems? *Am J Surg*. 2018;215:586–592.
12. Tiwari MM, Reynoso JF, Tsang AW, Oleynikov D. Comparison of outcomes of laparoscopic and open appendectomy in management of uncomplicated and complicated appendicitis. *Ann Surg*. 2011;254:927–932.
13. Mentula P, Sammalkorpi H, Leppäniemi A. Laparoscopic surgery or conservative treatment for appendiceal abscess in adults? A randomized controlled trial. *Ann Surg*. 2015;262:237–242.
14. Yau KK, Siu WT, Tang CN, Yang GP, Li MK. Laparoscopic versus open appendectomy for complicated appendicitis. *J Am Coll Surg*. 2007;205:60–65.
15. Ball CG, Kortbeek JB, Kirkpatrick AW, Mitchell P. Laparoscopic appendectomy for complicated appendicitis: an evaluation of postoperative factors. *Surg Endosc*. 2004;18:969–973.
16. Yu MC, Feng YJ, Wang W, Fan W, Cheng HT, Xu J. Is laparoscopic appendectomy feasible for complicated appendicitis ?A systematic review and meta-analysis. *Int J Surg*. 2017;40:187–197.